Supporting Information:

Functionally Important Aromatic-Aromatic and Sulfur- Interactions in the D2 Dopamine Receptor

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Table S1. Conventional mutagenesis of D2R

Mutant (D2R)	EC50 (μM)	Hill	n	Fold Shift
Wild type	0.020 +/- 0.001	1.2 +/- 0.1	15	-
C3.36A	0.49 +/- 0.03	1.1 +/- 0.1	16	25
C3.36K		No response		
C3.36L		No response		
C3.36M		No response		
C3.36S	0.67 +/- 0.04	1.1 +/- 0.1	17	34
T3.37A	1.9 +/- 0.2	1.0 +/- 0.1	13	95
T3.37C	2.1 +/- 0.1	1.1 +/- 0.1	13	105
T3.37S				
T3.37V		No response		
S5.46A		No response		
S5.46C	2.4 +/- 0.1	1.1 +/- 0.1	14	120
F5.47A	1.6 +/- 0.2	0.9 +/- 0.1	14	80
F5.47W	0.34 +/- 0.1	1.3 +/- 0.1	12	17
F5.47Y	0.051 +/- 0.004	1.3 +/- 0.1	10	3
Y5.48A	0.50 +/- 0.02	1.1 +/- 0.01	17	25
Y5.48F	0.020 +/- 0.001	1.0 +/- 0.1	4	0
Y5.48W		No response		
F5.51A	0.47 +/- 0.2	1.1 +/- 0.1	11	24
F5.51W	0.045 +/- 0.003	1.2 +/- 0.1	12	23
F5.51Y	0.0051 +/- 0.007	1.1 +/- 0.1	9	0.26
F6.44A	0.018 +/- 0.002	1.3 +/- 0.1	6	0.9
W6.48A		No response		
W6.48F	3.4 +/- 0.1	1.0 +/- 0.1	16	170
W6.48Y	0.65 +/- 0.04	1.0 +/- 0.1	17	33
F6.51A	> 100		10	>5000
F6.51W		No response		
F6.51Y	0.11 +/- 0.01	1.2 +/- 0.1	10	6
F6.52A	0.071 +/- 0.003	1.4 +/- 0.1	19	4
F6.52W	160 +/- 7	0.9 +/- 0.1	12	8000
F6.52Y	2.6 +/- 0.9	0.9 +/- 0.1	15	130
C3.36S/F5.47A	12 +/- 1	1.2 +/- 0.1	14	600
C3.36S/W6.48F	8.1 +/- 0.4	1.0 +/- 0.1	18	405
C3.36S/W6.48Y	2.1 +/- 0.1	1.0 +/- 0.1	15	105
T3.37C/S5.46C	2.0 +/- 0.1	1.1 +/- 0.1	17	100
F5.47A/Y5.48A	18 +/- 1	1.2 +/- 0.1	12	900
F5.47A/F5.51A	5.7 +/- 0.2	1.0 +/- 0.1	11	285
F5.47A/F6.52A	125 +/- 9	1.3 +/- 0.1	18	6250
F5.51A/F6.52A	4.6 +/- 0.1	1.1 +/- 0.1	16	230

Table S2. Conventional mutagenesis of D4R

Mutant (D4R)	EC50 (μM)	Hill	n	Fold shift	Ω	ΔΔG (kcal/mol)
Wild type	0.028 +/- 0.001	1.4 +/- 0.1	17	-		
F5.48A	0.016 +/- 0.001	1.4 +/- 0.1	12	0.6		
C5.51F	0.023 +/- 0.002	1.5 +/- 0.1	14	0.8		
C3.36S	0.017 +/- 0.001	1.4 +/- 0.1	13	0.6		
W6.48F	0.37 +/- 0.01	1.3 +/- 0.1	12	13		
W6.48Y	0.40 +/- 0.01	1.1 +/- 0.1	15	14		
C3.36S/W6.48F	0.28 +/- 0.01	1.3 +/- 0.1	13	10	1.2	0.1
C3.36S/W6.48Y	0.51 +/- 0.03	1.2 +/- 0.1	12	18	2.1	0.4
D3.32E	2.7 +/- 0.1	0.9 +/- 0.1	13	100		
D3.32N	230 +/- 14	1.2 +/- 0.1	10	8200		

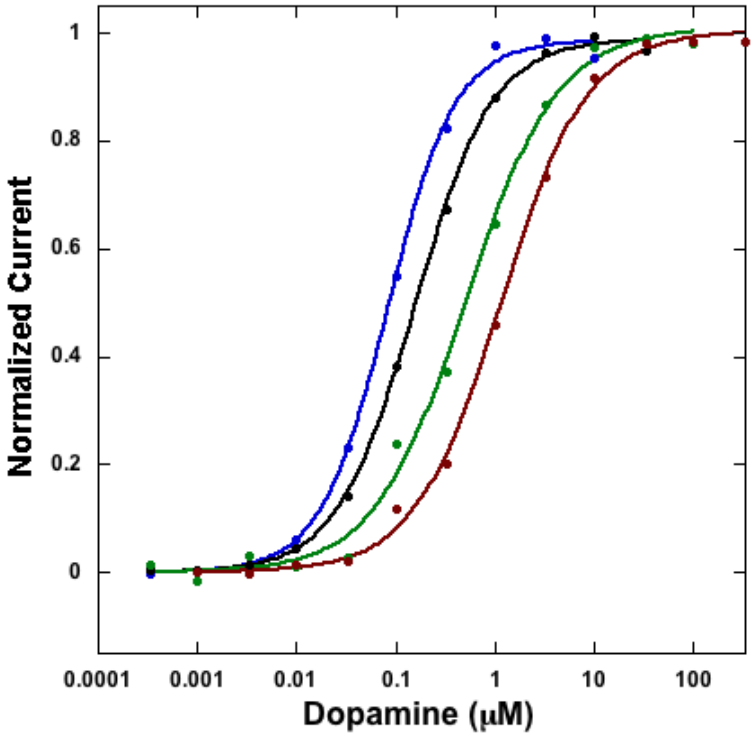

Figure S1. EC_{50} curves for D2R Y5.48Phe, F_1Phe, F_2Phe, and F_3Phe, respectively. Data was fit using the Hill equation.

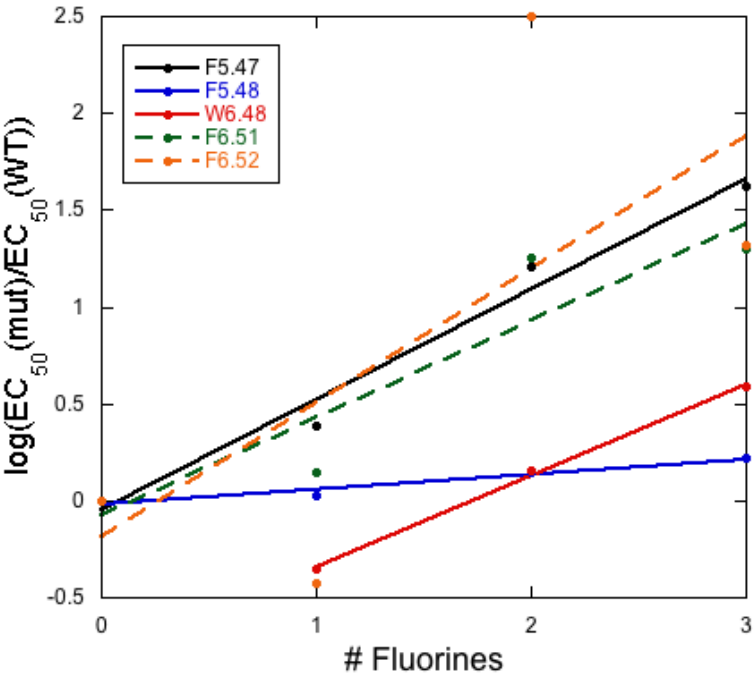

Figure S2. Fluorination trends of aromatic residues in the D4R. Solid lines represent residues showing a linear fluorination trend, dotted lines indicate poor fitting to a linear equation.

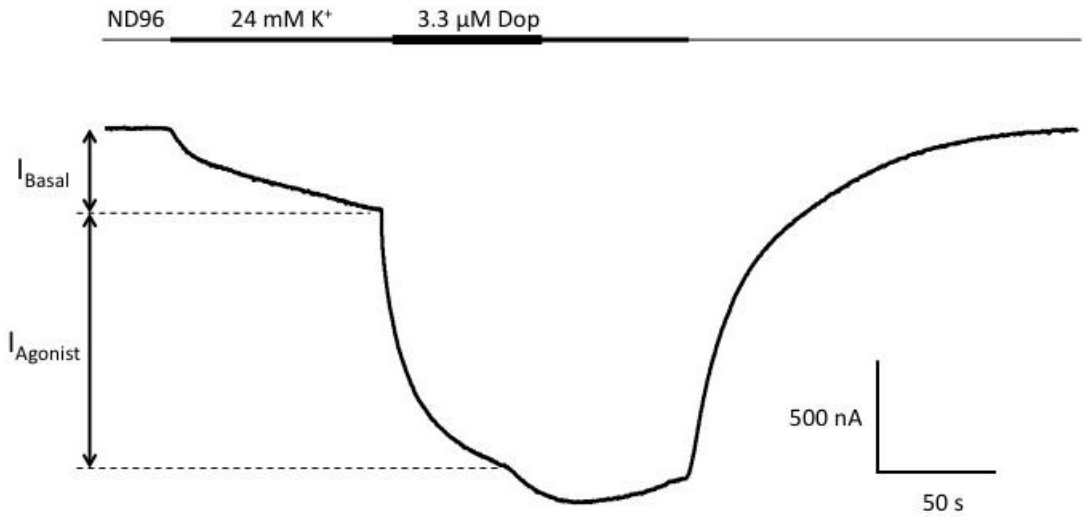

Figure S3. Sample trace of D2R wild type receptors expressed in *Xenopus laevis* oocytes with a 3.3 µM dopamine application. An EC_{50} curve was created by measuring the current ($I_{agonist}$) at varied dopamine concentrations, normalizing these values to the maximum $I_{agonist}$ value, and fitting the data to the Hill equation. Basal currents are caused by free $G_{\beta\gamma}$ in the cell activating the GIRK1/4 channels and were not included in data analysis.